REMARKS/ARGUMENTS

In response to the Office Action of February 24, 2006, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Status/Support for Amendments

Claims 1, 3 and 7 have been amended. Claims 4-6 have been cancelled. Claims 1-3 and 7-9 are currently under examination and remain pending in the application.

No new matter has been added by the amendments to the specification made herein.

The paragraph at page 12, beginning at line 18 was amended to clarify the international symbol in a proper name (~~Gaczy□ska~~ Gaczyńska).

The section entitled "Antibodies" has been amended to perfect compliance with the deposit rules (37 CFR 1.801-1.809) and to clarify that the BioAtlantic company is located in France.

No new matter has been added by the amendments to the claims made herein.

Claim 1 has been amended to clarify that the claimed method provides an assay for identification of an abnormal, truncated glycophorin that differs in structure and molecular weight from

normal glycophorin which is diagnostic for congestive heart failure (CHF). This fragment is theorized to be a fragment cleaved from the red blood cell surface during the disease process. Support for this clarification is found throughout the specification as originally filed, see, for example, page 4, lines 9-21, page 8, lines 12-21, page 14, lines 13-24, page 16, line 11 to page 18, line 22, page 20, line 13 to page 25, line 6, Figures 1, 2 and 4-6, and the claims as originally filed.

Claim 3 has been amended to include the information recited in claims 4 and 5 as originally filed.

Claim 7 has been amended for correct antecedent basis to claim 1. Claim 7 has also been amended for consistent lettering of steps.

Deposit

The Examiner notes that with respect to claims 3-5, it is apparent that the 3F4, 5F4 and 6G4 antibodies are required to practice the claimed invention.

As a required element, it must be known and readily available to the public or obtainable by repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line/hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest treaty, applicant is required to satisfy that all restriction imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in US patent applications. (emphasis added by the Examiner).

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for the deposit and maintenance of each deposit.

Applicant is reminded that the current address of the ATCC depository is: American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209. Applicants should amend the specification accordingly.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in the which case the statement need not be verified. See MPEP 1.804(b).

Applicants respectfully draw the Examiner's attention to the

section of the instant specification entitled "Antibodies" at pages 15 and 16.

The mouse monoclonal anti-glycophorin antibodies (3F4, 6G4 and 5F4) used to practice the claimed methods can be purchased from BioAtlantic, a French company specializing in immunological and immuno-haematological reagents (see the attached pages, translated and printed from their web site; reference 1). The specification has been amended herein to indicate that BioAtlantic is located in Nantes Cedex, France (page 15, lines 16-17).

Additionally, Hybridoma NaM26-3f4 D11A2, the hybridoma which produces the 3F4 monoclonal antibody used in the practice of the claimed methods, was deposited with the American Type Culture Collection under Accession Number PTA-5154 on April 23, 2003 (see the specification at page 16, beginning at line 4 and the attached copy of Receipt of Deposit; reference 2). The specification has been amended herein to indicate that Applicants will irrevocably remove any restrictions on the availability to the public of the deposited material upon granting of a US patent (see paragraph at page 16, beginning at line 4, as amended herein).

Thus, it is respectfully submitted that the antibodies (3F4, 6G4 and 5F4) which are required to practice the claimed methods are known and publically available. Accordingly, Applicants respectfully submit that the instant application is in compliance

with the deposit rules (37 CFR 1.801-1.809).

Rejection under 35 USC 112, second paragraph

Claims 1-9, as originally presented, stand rejected under 35 USC 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts that with respect to claim 1, step (b), the language wording "detecting said antibody-antigen binding complex wherein the presence of said antibody-antigen binding complex is diagnostic for congestive heart failure" is not clear. Merely "presence" alone is not indicative because the specification demonstrates that the healthy ones also have certain levels, albeit lower than congestive heart failure ones, of the complex in the range of 0.35 to 0.45 absorbance ratio. The Examiner asserts that Applicant needs to clarify.

Claim 1 has been amended herein to clarify that a statistically significant increase in an antibody-antigen binding complex formed by the monoclonal antibody of step (a), the 3F4 monoclonal antibody, as compared with the amount of antibody-antigen complexes formed by the monoclonal antibodies of steps (b) and (c) in biological fluid samples is diagnostic for congestive heart failure.

Accordingly, Applicants have now clarified the metes and bounds of the claims and respectfully request that the above-discussed rejection under 35 USC 112, second paragraph be withdrawn.

Rejections under 35 USC 103(a)

Claims 1, 2 and 6, as originally presented, stand rejected under 35 USC 103(a) as allegedly being unpatentable over Goldman et al. (Modern Pathology 14(6):589-594 2001).

Goldman et al. is deemed by the Examiner to teach a pathological analysis of examining of myocardial infarction patients. Goldman et al. determine various biological markers from the patients' plasma sample, including glycophorin A antigen (see abstract; page 589, right column, last paragraph). Goldman et al. discover that the patients have symptoms of erythropoiesis confirmed by immunostaining with antibody to glycophorin (see Figure 1, H). However, Goldman et al. do not explicitly teach measuring the complex of glycophorin-antibodies as an indicator for diagnostic of congestive heart failure.

Nevertheless, Goldman et al. discuss the correlation of the congestive heart failure with the myocardial infarction (page 589, right column, first paragraph). Also Goldman et al. report the correlation of congestive heart failure with the erythropoiesis

(see page 589, right column, first paragraph).

Therefore, the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time that the invention was made to have motivated Goldman et al. to further determine the correlation between congestive heart failure with the level of glycophorin in the suspected patients with reasonable expectation of success because it is known that the glycophorin antigen can be detected in erythropoiesis, and a potential relationship between congestive heart failure and erythropoiesis has been established.

Applicants respectfully disagree with all of the Examiner's assertions.

The instantly claimed invention is a method for diagnosing congestive heart failure by identifying an increased presence of an abnormal, truncated glycophorin antigen in the bodily fluid of an individual.

The Examiner is reminded that in order to establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations (MPEP 2142).

Goldman et al. investigated myocardial hematopoiesis in patients with heart failure due to myocardial infarction. The hematopoiesis was identified based on characteristic light-

microscope findings in routinely processed tissue confirmed by immunohistochemistry using monoclonal antibodies to the erythroid cell marker glycophorin A. Thus, the glycophorin antigen identified by Goldman et al. was a normal component of the membrane of red blood cells found in heart tissue (see abstract and Methods section). In contrast to the instant invention, Goldman et al. do not teach or suggest the identification of glycophorin in plasma or in any other bodily fluid.

Furthermore, Goldman et al. refer only to glycophorin as an erythroid cell marker and do not teach or suggest any other alternative and/or abnormal forms of glycophorin.

The information known in the art does not remedy the deficiencies of Goldman et al. since glycophorin was not recognized as a marker for congestive heart failure prior to the instant invention.

Thus, neither Goldman et al. singly or combined with information known in the prior art, teach or suggest all of the limitations of the methods as instantly claimed.

In light of all of the above remarks, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness and further contend that a medical professional and/or biologist of ordinary skill in the art, having the reference (Goldman et al.) in front of him/her would not have the information

and motivation necessary to arrive at Applicants' invention.

Thus, it is respectfully submitted that the combination of Goldman et al. and information known in the prior art fails to reasonably teach or suggest to one of ordinary skill in the medical/biological arts the elements of Applicants' methods as specifically set forth in claims 1-3 and 7-9, as presented herein.

Accordingly, Applicants respectfully submit that the claimed methods distinguish over the prior art and respectfully request that this rejection under 35 USC 103(a) now be withdrawn.

Claims 7-9, as originally presented, stand rejected under 35 USC 103 (a) as allegedly being unpatentable over Goldman et al. (Modern Pathology 14(6):589-594 2001) in view of Mak (US 6,190,691).

The Examiner asserts that the Goldman et al. reference has been discussed but does not explicitly teach using a second antibody attached with a label to detect the complex of the glycophorin-antibody.

Mak is deemed by the Examiner to teach modified ELISA using a labeled second antibody recognizing a first antigen-antibody complex to increase detection sensitivity and specificity (column 16, lines 32-50).

Therefore, the Examiner concludes that it would have been

obvious to one of ordinary skill in the art at the time that the invention was made to have provided Goldman et al. with a labeled second polyclonal antibody specific for the antigen-antibody complex as taught by Mak in order to increase sensitivity and specificity because such technique is well known and widely practiced in the art.

The Examiner asserts, with respect to claims 8 and 9, Mak teach labeling the second antibody with peroxidase as the signal generating substance (column 16, lines 45-50).

The scope of the teachings of Goldman et al. is as discussed above in the response to the first rejection under 35 USC 103(a).

The teachings of Mak do not remedy the deficiencies of Goldman et al. since Mak teaches nothing about congestive heart failure or glycophorin.

Thus, neither Goldman et al. nor Mak singly or combined, teach or suggest all of the limitations of the methods as instantly claimed.

The information known in the art does not remedy the deficiencies of Goldman et al. and/or Mak since glycophorin was not recognized as a marker for congestive heart failure prior to the instant invention.

In light of all of the above remarks, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case

of obviousness and further contend that a medical professional and/or biologist of ordinary skill in the art, having the references (Goldman et al. and Mak) in front of him/her would not have the information and motivation necessary to arrive at Applicants' invention.

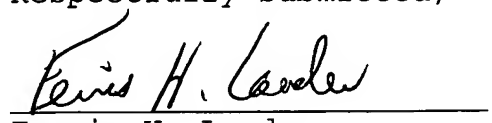
Thus, it is respectfully submitted that the combination of Goldman et al., Mak, and information known in the prior art fails to reasonably teach or suggest to one of ordinary skill in the medical/biological arts the elements of Applicants' methods as specifically set forth in claims 1-5 and 7-9, as presented herein.

Accordingly, Applicants respectfully submit that the claimed methods distinguish over the prior art and respectfully request that this rejection under 35 USC 103(a) now be withdrawn.

CONCLUSION

In light of the foregoing remarks, amendments to the specification and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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